## Table S1. The top 15 up-regulated genes after acute FGF23 administration

| Gene Name                                    | Symbol  | NCBI No.  | Fold Change | P-value  |
|--|---------|-----------|-------------|----------|
| Early growth response 1                      | Egr1    | NM_007913 | 9.06671     | 1.36E-08 |
| Heparin-binding EGF-like growth factor       | Hbegf   | NM_010415 | 3.09658     | 5.33E-05 |
| Dual specificity phosphatase 6               | Dusp6   | NM_026268 | 2.41652     | 1.65E-08 |
| Zinc finger protein 36                       | Zfp36   | NM_011756 | 2.22423     | 0.00017  |
| Immediate early response 2                   | Ier2    | NM_010499 | 1.96741     | 8.97E-06 |
| Dual specificity phosphatase 4               | Dusp4   | NM_176933 | 1.87764     | 0.000835 |
| Basic helix-loop-helix domain, class B2      | Bhlhb2  | NM_011498 | 1.79652     | 0.000678 |
| Ngfi-A binding protein                       | Nab2    | NM_008668 | 1.69864     | 0.000396 |
| Jun-B oncogene                               | Junb    | NM_008416 | 1.65532     | 0.000384 |
| SERTA domain containing 1                    | Sertad1 | NM_018820 | 1.50534     | 6.02E-05 |
| Choline kinase alpha                         | Chka    | NM_013490 | 1.50023     | 0.000239 |
| DnaJ (Hsp40) homolog, subfamily C, member 17 | Dnajc17 | NM_139139 | 1.48847     | 0.000155 |
| DNA-damage inducible transcript 3            | Ddit3   | NM_007837 | 1.48731     | 0.000251 |
| Sprouty homolog 2                            | Spry2   | NM_011897 | 1.47345     | 0.000733 |
| FBJ osteosarcoma oncogene                    | Fos     | NM_010234 | 1.4645      | 0.000658 |

## Table S2. The 15 most down-regulated genes after acute FGF23 administration

| Gene Name   | Symbol  | NCBI No.     | Fold Change | P-value  |
|---|---------|--------------|-------------|----------|
| Acyl-CoA thioesterase 3                             | Acot3   | NM_134246    | -1.44409    | 0.000438 |
| Solute carrier organic anion transporter family     |         |              |             |          |
| member 1a4  | Slco1a4 | NM_030687    | -1.43617    | 0.000374 |
| Solute carrier family 35                            | Slc35a3 | NM_144902    | -1.35772    | 0.000985 |
| Leucine-rich repeats and immunoglobulin-like        |         |              |             |          |
| domains 2   | Lrig2   | NM_001025067 | -1.33814    | 0.000991 |
| APOBEC1 complementation factor                      | Alcf    | NM_001081074 | -1.33433    | 0.000139 |
| Tetratricopeptide repeat domain 30A2                | Ttc30a2 | NM_001081228 | -1.31536    | 0.000198 |
| Tryptophan rich basic protein                       | Wrb     | NM_207301    | -1.29465    | 2.62E-05 |
| ATPase, H+ transporting, lysosomal accessory        |         |              |             |          |
| protein 2   | Atp6ap2 | NM_027439    | -1.28521    | 0.000426 |
| Solute carrier family 31, member 1                  | Slc31a1 | NM_175090    | -1.27627    | 0.000518 |
| Calcium-dependent activator protein for secretion 2 | Cadps2  | NM_153163    | -1.2553     | 0.000982 |
| Carbonic anhydrase 13                               | Car13   | NM_024495    | -1.24159    | 0.000629 |
| Plasma glutamate carboxypeptidase                   | Pgcp    | NM_018755    | -1.22196    | 0.000821 |
| Adenosine deaminase-like                            | Adal    | NM_029475    | -1.20276    | 0.000991 |
| Galactose mutarotase                                | Galm    | NM_176963    | -1.19341    | 0.000266 |
| Germ cell-less homolog 1                            | Gmcl1   | NM_027955    | -1.17749    | 0.000901 |







Figure S2



Figure S3



**Table S1 and Table S2. Kidney microarray data after acute FGF23 administration.** By microarray, 1 hour post FGF23 injection to WT mice showed significant changes in kidney mRNAs compared with control mice. The top 15 up-regulated genes are listed in Table 1 with Egr1 serving as the positive control for FGF23 signaling through MAPK. Hbegf was the second-most highly elevated gene. Table 2 lists the 15 most down-regulated genes.

**Figure S1. Violin plots of nephron segment gene markers.** Violin plots of (A) Npt2a (primarily proximal tubule) and (B) Ncc (primarily distal tubule) are shown.

**Figure S2. Long term effect of HBEGF on WT renal genes.** 5 ug rhHBEGF was given intravenously to 9-10 week old female WT mice. (A) Egr1 mRNA expression was induced at 3 h and returned to baseline level at 9 h and 13 h. No significant changes were observed in serum phosphorus (B). (\*P<0.05 versus saline control mice. N=4-5. 'Sal', saline).

**Figure S3. Incremental doses of HBEGF** *in vitro*. HEK293 cells were treated with saline (Ctrl), 0.1 ng/ml, 1 ng/ml, 5 ng/ml, 10 ng/ml, 50 ng/ml or 100 ng/ml of rhHBEGF for 24 h. (A) EGR1 mRNA levels started increasing at 5 ng/ml and were significantly elevated at 50 ng/ml and 100 ng/ml; (B) CYP24A1 showed a similar pattern; (C) CYP27B1 was significantly decreased at 50 ng/ml and 100 ng/ml (\*P<0.05, \*\*P<0.01 versus the bracketed groups. N=3).

Supplementary information is available at *Kidney International*'s website.